REMARKS

I. Support for the Amendments to the Claims

Claims 1-15, 17-18, 20-35 and 66 are currently in the application. Claims 1, 2, 4, 5, 22, 35, and 66 have been amended. The amendments to claims 1, 2, 4, 5, 22, 35, and 66 are made without prejudice to pursuit of the previous claims in an appropriate divisional or continuation application.

Support for the amendments to claims 1, 2, 4, 5, 22, 35, and 66 can be found throughout the specification and claims as originally filed. No new matter has been added by the amendments to the claims.

Additional support for the amendments to claims 1, 2, 4, 5, 22, 35, and 66 can be found, e.g., in the language of the original claims and in the specification, e.g., on page 11, lines 9-12; in the Examples (especially on page 32, lines 5-7 and 14-32; on page 35, lines 18-29; on page 37, lines 6-18; from page 37, line 34, to page 38, line 17; on page 39, lines 8-20; and on page 40, lines 1-17); and in the Abstract.

II. Status of the Claims

Claims 1-15, 17-18, 20-35 and 66 are currently in the application. Claims 1, 2, 4, 5, 22, 35, and 66 have been amended.

III. The Rejection of Claims 1-12, 14-15, 17-18, 20-21, 23-35 and 66 under 35 U.S.C. §103(a) over Smith in View of Mitchell and Burgoyne is Traversed

The Examiner has rejected claims 1-12, 14-15, 17-18, 20-21, 23-35, and 66 under 35 U.S.C. 103(a) as allegedly unpatentable over Smith et al. (U.S. Patent 6,645,717; issued November 11, 2003; "Smith") as evidenced by Burgoyne (U.S. Patent 5,496,562; issued March 5, 1996; "Burgoyne") and Mitchell et al. (WO 00/21973; published April 20, 2000; "Mitchell"). Applicants traverse the rejection and respectfully request reconsideration of these claims.

The Patent Office alleges that with respect to independent claims 1, 35, and 66, Smith teaches a method for isolating and storing nucleic acid comprising steps a, d, b, c, e, f, and g, ***in that order***.

The Patent Office alleges, in pertinent part:

> Smith et al. do **not** teach that the solution of step (d) is applied to the support ***subsequently*** to immobilization of cells onto the support. However, as evidenced by Mitchell et al., the order of steps can be reversed, leading to the same end result, i.e. nucleic acid from lysed cells immobilized onto a filter (see Mitchell et al. page 2, third paragraph)...[P. 4; all emphasis added.]

The Patent Office also alleges, in pertinent part:

> Smith et al. do **not** specifically teach removing contaminants from immobilized cells before cell lysis. However, washing cells before lysis to obtain genetic material is well estabilished in the art at the time of the invention. Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have added a cell-washing step in the method of Smith et al., since such wash would improve quality of nucleic acid obtained from the cells. [P. 8.]

The Patent Office then cites *Ex parte Rubin*, 128 USPQ 440 (Bd. App. 1959) ("*Rubin*"), *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) ("*Burhans*"), and *In re Gibson*, 39 F.2d 975, 5, USPQ 230 (CCPA 1930) ("*Gibson*"), as well as the Manual of Patent Examining Procedure ("MPEP") §2111.01 II with attention drawn to *Altiris, Inc. v. Symantec*

Corp., 318 F.3d 1363, 1371, 65 USPQ2d 1865, 1869-70 (Fed. Cir. 2003) ("*Altiris*") before concluding:

> Therefore it would have been prima facie obvious to one of ordinary skill in the art to reverse the order of steps in the method of Smith et al., since the end result is still the same. [P. 5.]

A. The Order of the Steps is Shown in the Claims and Specification

The Patent Office cites the MPEP §2111.01 (and its description of *Altiris*, 318 F.3d at 1371, 65 USPQ2d at 1869-70) for the following proposition:

> Although the specification discussed only a single embodiment, the court held that it was improper to read a specific order of steps into method claims where, as a matter of logic or grammar, the language of the method claims did not impose a specific order on the performance of the method steps, and the specification did not directly or implicitly require a particular order. [P. 5, *citing* MPEP §2111.01, *citing Altiris, Inc. v. Symantec Corp.*, 318 F.3d 1363, 1371, 65 USPQ2d 1865, 1869-70 (Fed. Cir. 2003).]

Unlike *Altiris*, however, the claims and specification demonstrate that the steps have an express order (*Altiris, Inc. v. Symantec Corp.*, 318 F.3d at 1371, 65 USPQ2d at 1869-70).

The Patent Office has clearly chosen to ignore the previous language of the claims (previously "subsequently") and the arguments previously made, and accepted, in support thereof.

In addition, the present claim language, which is well-supported in the specification for reasons already made of record, likewise supports the order of the steps.

In brief, Applicants submit that this language is amply supported by the specification and the claims as originally filed.

First, claims 1, 35, and 66 are method claims reciting a series of steps, which would imply to one of ordinary skilled in the art, who is familiar with laboratory protocols, that the steps are sequential, similar to a lab protocol or recipe. Although the word "comprising" is used, the amendments to the claims with the term "subsequent" (previously "subsequently") provide order to the steps.

In particular, the specification states:

> The present method provides a quick, simplified, cost effective method for storing, and ***subsequently*** isolating, nucleic acids using a wide range of commercially available solid phase media, which until now have been considered inappropriate for storage....[P. 11, ll. 9-12; emphasis added.]

Second, the language of the Examples with respect to the protocol clearly indicates the sequential order of the method steps of claims 1, 35, and 66. The Examiner's attention is directed to the initial paragraph, particularly to the following:

> ....25-50 µl FTA® solution (Whatman) were applied to each column ***after*** Nucleated Cell Capture and Red Cell Lysis Step. ***Then*** columns were left at room temperature for drying, storage and subsequent DNA extraction. [P. 32, ll. 5-7; all emphasis added.]

The Examiner's attention is also directed to the "Study design for Examples 1-4" (p. 32, ll. 14-32), the "Study design" for Example 5 (p. 35, ll. 18-29), the "Study design" for Example 6 (p. 37, ll. 6-18), the "Study design" for Example 7 (p. 37, l. 34, to p. 38, l. 17), the "Study design" for Example 8 (p. 39, ll. 8-20), and the "Study design" for Example 9 (p. 40, ll. 1-17) with respect to filters/media of various types. One of ordinary skill in the art would understand that the steps in these laboratory protocols (Examples with actual reduction to practice) were intended to be performed in their stated order.

In the "Study design for Examples 1-4" (p. 32, ll. 14-32), the laboratory protocol has the following ordered steps: (i) application of human whole blood onto the column; (ii) washing of the column with a red-cell lysis buffer; (iii) application of lysis solution to the column; (iv) drying of the column; (v) storage of the column; (vi) isolation of DNA from the column; and (vii) evaluation of the DNA quality and quantity.

In the "Study design" for Example 5 (p. 35, ll. 18-29), the laboratory protocol has the following ordered steps: (i) application of blood onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control); (iv) storage of the column at ambient conditions; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 6 (p. 37, ll. 6-18), the laboratory protocol has the following ordered steps: (i) application of whole blood onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 7 (p. 37, l. 34, to p. 38, l. 17), the laboratory protocol has the following ordered steps: (i) application of whole blood onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 8 (p. 39, ll. 8-20), the laboratory protocol has the following ordered steps: (i) application of whole blood onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no

application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In the "Study design" for Example 9 (p. 40, ll. 1-17), the laboratory protocol has the following ordered steps: (i) application of white blood cells onto the column; (ii) washing of the column with a washing solution; (iii) application of lysis solution to the column (with no application of lysis solution to the control group); (iv) drying and storing of the column; (v) isolation of DNA from the column; and (vi) evaluation of the DNA quality and quantity.

In each instance, the Study Design fully describes the ordered steps of claims 1, 35, and 66 in the order described in those claims. Similar support can be found in the Abstract as originally filed in PCT/US2003/031483 (filed October 3, 2003), of which the present application is a national phase application.

B. The Claimed Invention Would Not Have Been Obvious

The Patent Office then cites *Ex parte Rubin*, 128 USPQ 440 (Bd. App. 1959) ("*Rubin*"), *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) ("*Burhans*"), and *In re Gibson*, 39 F.2d 975, 5, USPQ 230 (CCPA 1930) ("*Gibson*"), as well as the Manual of Patent Examining Procedure ("MPEP") §2111.01 II with attention drawn to *Altiris, Inc. v. Symantec Corp.*, 318 F.3d 1363, 1371, 65 USPQ2d 1865, 1869-70 (Fed. Cir. 2003) ("*Altiris*") before concluding:

> Therefore it would have been prima facie obvious to one of ordinary skill in the art to reverse the order of steps in the method of Smith et al., since the end result is still the same. [P. 5.]

Applicants respectfully disagree and traverse this rejection for the reasons discussed during the Telephonic Interview on January 14, 2010, and in the previous prosecution and for the following reasons.

In essence, a key difference between Smith and the present invention is that in Smith, the chemical composition is deposited on the support and dried and then is contacted by a cellular sample, whereas in the present invention, the solution is applied to the solid matrix after the matrix contains the sample.

Unlike a simple mechanical method, however, the **divergent methods** of Smith/Burgoyne and Mitchell and the methods of the present invention involve interactions with nucleic acid, which would ***not be predictable***. While according to the Federal Circuit, one of ordinary skill in the art might have expected the same product to result from the process in *Rubin*, regardless of the order of steps, that same expectation would not hold when changing the order of steps in a sequential, multi-step biotechnology process for nucleic acids.

This lack of predictability can easily supported by the fact that the disclosure of Mitchell ***directly contradicts*** that of Smith, which in fact, actually demonstrates this lack of predictability given that one reference (Smith) describes isolation of nucleic acids on a dry, coated membrane, while the other reference (Mitchell) expressly asserts the necessity of preventing dryness of the solid support in order to avoid nucleic acid shearing.

Applicants wish to point out the advantages of the present invention and that, contrary to the Examiner's assertion, the end result is ***not*** necessarily the same.

As a practical matter, the filter of Smith can only contain a finite amount of the coating solution, because only so much solution can adsorb to the support, which also limits the number of cells that can be lysed by the finite amount of solution. Moreover, the addition of a biological sample to the filter of Smith would, in most instances, reduce the local

concentration of the coating (given that a biological sample – even a solid – typically includes water, as earth-based life forms include water).

In contrast, using the present invention, the cells can be concentrated in the medium prior to application of indefinite amounts of solution (see, e.g., claims 35 and 66).

In addition, ***all*** the cell types in a mixed cell sample placed on the filter of Smith would be expected to be lysed upon contacting the filter, whereas in the method of the present invention, cells of a ***desired*** cell type can be ***isolated*** on the solid phase medium and the other cells removed prior to application of the solution and lysis of the entrapped cells of ***only the desired cell type***.

Nothing in Smith would suggest to one of skill in the art that it would produce the present invention (solution application following sample application and subsequent drying). In contrast, in the present invention, ***the sample is added to the solid phase medium first and then the solution*** (comprising (i) an anionic surfactant or detergent, (ii) a weak base, and (iii) a chelating agent; step d), ***followed by drying and storage***. Therefore, the present invention is distinguishable from Smith.

Applicants respectfully submit that Mitchell and/or Burgoyne fail to supply the deficiencies of Smith.

In the present language of claim 1, the sample is added to the solid phase medium first and then the solution (comprising a weak base, a chelating agent, and an anionic surfactant or detergent). (Similarly, in Smith and Burgoyne, one solution is applied as a chemical coating to the support to form the filter.) Therefore, the ***present invention*** is distinguishable in that ***one solution*** is added to the sample and ***not multiple solutions added sequentially as in Mitchell***.

Another distinction is the drying of the sample for storage and archiving of DNA. Mitchell states (p. 7, ll. 15-20) that if the filter is allowed to dry, the DNA is recoverable but sheared and, where the method is carried out in a column, indicates the need for using a vapor block to prevent drying from occurring, because this is undesirable. ***Such a method is in contrast to the present invention, in which the medium is dried without shearing (unlike Mitchell, in which drying is equated with shearing).***

Therefore, Mitchell teaches away from both the present invention and Smith and/or Burgoyne. One of ordinary skill in the art would not have been motivated to combine Mitchell with Smith and/or Burgoyne, and such a combination would not have been expected to produce the present invention. If Mitchell had read Smith and/or Burgoyne, he would surely have assumed that it was impossible to dry out his column ***unless*** he had ***pre*-protected** his column material to prevent it from degrading the DNA. It is the present invention which – ***surprisingly*** – showed that one did not need to protect the column beforehand, but that one could include the necessary protecting and lysing agents all in one solution and ***subsequently*** apply this to the already trapped nucleic acid-containing cells. It is ***surely quite surprising*** that enough of the protecting agents will stick on the column to prevent degradation and allow one to dry out the material for elution at a later stage. It is also very practical, because one can defer the point at which one needs to isolate and test the DNA itself.

Moreover, in Mitchell, the SDS and TE are not part of the same solution, but the current claim 1 is directed to "a solution comprising (i) an anionic surfactant or detergent, (ii) a weak base, and (iii) a chelating agent." In Mitchell, the SDS and TE are added separately and filtered to waste.

Mitchell uses a lysis buffer (such as a detergent) to lyse the cells, but then follows this step with a low salt buffer (e.g., TE^{-1} or water) (see pp. 7-8, 14-15; see also Example 1 [p. 18: lysis by 0.5% SDS, followed by washing with TE]). The effect of this second wash, however, is to wash out any remaining anionic detergent, which as noted by Dr. Walter King

during the Telephonic Interview on January 14, 2010, would remove the anions, leaving the isolated nucleic acid unprotected after drying and subject to degradation, unlike the present invention in which at least some portion of the anionic surfactant/detergent-containing solution is dried on the medium.

In addition, the present claims are directed to a method wherein the cell lysate comprises nucleic acid. While the specification of the present application also describes an alternative method including a separate lysis step for nuclei using a "low-salt, non-isotonic buffer, such as a hypotonic buffer" (see, e.g., page 17, lines 1-29), the present claims are directed to the use of an anionic surfactant or detergent, which "increases the yield and purity of the DNA product" the use of which results in the nucleic acid being "retained by the media" (see, e.g., page 16, lines 7-29, and page 17, line 31).

Nothing in Mitchell would suggest to one of skill in the art that it should be combined with Smith, or *vice versa*, to produce the present invention (single solution application following sample application and subsequent drying for archiving). ***In particular, one of skill in the art would not cite Mitchell's method for archiving since Mitchell specifically teaches away from drying, as it harms the nucleic acid and reduces yield.***

Specifically, in Mitchell, ***multiple lysis solutions*** are added ***sequentially*** in order to function, and Mitchell ***teaches away from drying***, as it **shears the nucleic acid** and **reduces yield**. Smith and Burgoyne use a chemical composition of the base, chelator, detergent and uric acid/urate salt ***that is already deposited*** on the solid matrix ***and dried prior to exposure*** to the cells.

In contrast, in the present language of underlying claim 1, ***the sample is added to the solid phase medium first and then the single-solution archiving agent*** (a solution comprising (i) an anionic surfactant or detergent, (ii) a weak base, and (iii) a chelating agent;

step d), ***followed by drying and storage***. Therefore, the present invention is distinguishable from both Mitchell and Smith, either alone or in combination with one another.

Moreover, for the reasons discussed above, not only do the teachings of Mitchell and/or Burgoyne fail to supply the deficiencies of Smith, the teachings of Mitchell and Smith/Burgoyne are incompatible and the two sets of references teach away from each other.

Applicants respectfully draw attention to the Examination Guidelines Update: Developments in the Obviousness Inquiry After *KSR v. Teleflex* (Fed. Reg. 75[169]: 53643-53660 [Sept. 1, 2010] [hereinafter the "2010 Guidelines"]). In view of the teachings of Mitchell ***away from*** the teachings of Smith and/or Burgoyne, **the Patent Office has *failed* to show** that the present invention has in any way combined prior art elements according to known methods in Smith with Mitchell and/or Burgoyne to yield ***predictable*** results, or that this is a case of simple substitution of one known element for another to obtain ***predictable*** results, or the use or application of a known technique to improve a similar device or method in the same way. In view of the teachings of Mitchell ***away from*** the teachings of Smith and/or Burgoyne, **the Patent Office has *not* shown** that the present invention is the result of known work in one field of endeavor prompting a variation for use in the same field or in a different one based on either design incentives or other market forces ***predictable*** to one of ordinary skill in the art. In view of the teachings of Mitchell ***away from*** the teachings of Smith and/or Burgoyne, **the Patent Office has *not* shown** that the present invention is the result of ***predictable*** variation in Smith, either alone or in combination with Burgoyne, or that it resulted from the choice from a finite number of identified, ***predictable*** solutions having a reasonable expectation of success, ***nor* has it shown that it would have been obvious to try with a reasonable expectation of success** (e.g., "cell cycle-specifically differentiated hematopoietic cell type"). Moreover, in view of the teachings of Mitchell ***away from*** the teachings of Smith and/or Burgoyne, there is ***no teaching, suggestion, or motivation*** in Smith in view of Mitchell and/or Burgoyne that would have led one of ordinary skill in the art to modify Smith or Burgoyne to yield the methods of the present invention. (*Id.*)

While obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so, "**[t]he mere fact that references can be combined or modified does *not* render the resultant combination obvious *unless the results would have been predictable* to one of ordinary skill in the art**" (MPEP §2143.01 (underline in original; other emphasis added); *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S.Ct. 1727, 82 USPQ2d 1385, 1396 [2007]), and **the mere statement that the claimed invention is within the capabilities of one of ordinary skill in the art *does not suffice* to establish obviousness** (MPEP §2143.01; *see also KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d at 1396). The prior art can be modified or combined to establish *prima facie* obviousness, ***but one of ordinary skill in the art would have to have had a reasonable expectation of success or at least some degree of predictability at the time the invention was made*** (*In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 [Fed. Cir. 1986]; MPEP §2143.02).

With respect to MPEP §2143, the method of the present invention does **not** fall under the category of a simple substitution (*see, e.g., In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 [Fed. Cir. 1988]); it is **not** the result of predictable variation or the choice from a finite number of identified, ***predictable*** solutions having a reasonable expectation of success, **nor** would it have been obvious to try with a ***reasonable expectation*** of success (*see, e.g., Pfizer v. Apotex*, 480 F.3d 148, 82 USPQ2d 1321 [Fed. Cir. 2007]; *Ex parte Kubin*, 83 USPQ2d 1410 [Bd. Pat. App. & Inter. 2007]); **nor** was there any teaching, suggestion or motivation in Smith and/or Burgoyne, either alone or in combination with Mitchell, that would have led one of ordinary skill in the art to modify one or more of these references or to combine their teachings to result in the method of the present invention (MPEP §2143).

In the present invention, therefore the improvement is more that the predictable use of prior art elements according to their established functions.

Claims 12, 14-15, 17-18, 20-21, 23-34 are dependent, either directly or indirectly, on claim 1 as an underlying claim and the same reasoning applies to these dependent claims.

Further with respect to claims 23-24, the Patent Office alleges:

> Regarding claims 23-24, in the disclosure, Smith et al. teach different fibers for the filters (column 6, lines 32-40). [P. 7.]

This remark is irrelevant for claims 23-24, given that these claims do not recite filter fiber limitations, and Applicants respectfully traverse this rejection.

Further with respect to claim 27, the Patent Office alleges:

> Regarding claim 27, Smith et al. deppositing whole blood onto a filter (col. 10, liknes 42-45), therefore they inherently teach concentrating the cells in the solid phase medium. [P. 7.]

As a practical matter, the filter of Smith can only contain a finite amount of the coating solution, because only so much solution can adsorb to the support, which also limits the number of cells that can be lysed by the finite amount of solution. Moreover, the addition of a biological sample to the filter of Smith would, in most instances, reduce the local concentration of the coating (given that a biological sample – even a solid – typically includes water, as earth-based life forms include water).

In contrast, using the present invention, the cells can be concentrated in the medium prior to application of indefinite amounts of solution (see, e.g., claim 27), and Applicants respectfully traverse this rejection.

C. Improper Novelty Rejection

With respect to claim 24, Applicants respectfully assert that the Patent Office has made an improper novelty rejection.

The Patent Office alleges:

> ....As evidenced by Mitchell et al., binding of the nucleic acid to filters is generally non-ionic (page 9, third paragraph). Since the known non-ionic interactions include the ones listed in claim 24, and due to the compliexity of the system, at least one type of the interaction listed in claim 24 inherently occurs within DNA immobilized onto a membrane. For example, as stated by Mitchell et al. (page 9, first paragraph):
>
> "It is postulated that nucleic acid-nucleic acid interactions themselves are important in maintaining a sufficiently high cross-sectional area to retard movement of the nucleic acid through the filter".
>
> Since DNA-DNA interactions include at least hydrogen bonding and dispersion forces, the claim's limitations are ***anticipated***. [P. 7; all emphasis added.]

To anticipate a claim (35 U.S.C. §102(b)), a single prior art reference must teach each and every element of the claim (*Verdegaal Brs. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 [Fed. Cir. 1987]; MPEP §2131). "Every element of the claimed invention must be literally present, arranged as in the claim....The identical invention must be shown in as complete detail as is contained in the patent claim...." (*Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 [Fed. Cir. 1989] [citations omitted]; MPEP §2131).

Applicants note that among other steps, for example, Mitchell fails to describe drying step f, and in fact, teaches away from any drying step. Therefore, Mitchell fails to anticipate claim 24.

Applicants likewise submit that claim 24 is not obvious over any combination of Smith, Mitchell, and/or Burgoyne for the reasons discussed at length above.

Applicants respectfully submit that claims 1-12, 14-15, 17-18, 20-21, 23-35, and 66 fulfill the requirements of 35 U.S.C. §103(a), thereby placing these claims in condition for allowance, and request the Examiner's reconsideration accordingly.

IV. The Rejection of Claim 13 under 35 U.S.C. §103(a) over Smith in View of Mitchell, Burgoyne, and the Whatman Filter Paper Overview is Traversed

The Examiner has rejected claim 13 under 35 U.S.C. 103(a) as allegedly unpatentable over Smith et al. (U.S. Patent 6,645,717; issued November 11, 2003; "Smith") as evidenced by Burgoyne (U.S. Patent 5,496,562; issued March 5, 1996; "Burgoyne") and Mitchell et al. (WO 00/21973; published April 20, 2000; "Mitchell"), as applied to claims 1 and 10 above and evidenced by the Whatman filter paper overview ("downloaded from the internet on May 21, 2010"). Applicants traverse the rejection and respectfully request reconsideration of this claim.

The Patent Office alleges, in pertinent part:

> The teachings of Smith et al. are set forth in section 4 above. Smith et al. do not disclose the pore size from 0.2 um to 2.7 um.
>
> As evidenced by the range of filter materials and filters provided by Whatman, the filters have a variety of pore sizes between 0.015 to 12 microns. Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have picked a filter with pore size appropriate to the type of cells being lysed, for example. [P. 8.]

Applicants respectfully traverse this rejection.

Applicants note that the "Whatman filter paper overview" ("Membrane Filters") is described by the Patent Office as "downloaded from the internet on May 21, 2010." The

present application claims priority of U.S. Provisional Application 60/416,356, which was filed on October 4, 2002.

Therefore, the Patent Office has improperly cited the "Whatman filter paper overview," which post-dates the priority date of the present application.

For the reasons discussed at length above, Applicants also respectfully assert that claim 13 would not have been obvious to one of ordinary skill in the art over the remaining references.

Applicants respectfully submit that claim 13 fulfills the requirements of 35 U.S.C. §103(a), thereby placing this claim in condition for allowance, and request the Examiner's reconsideration accordingly.

V. The Rejection of Claim 22 under 35 U.S.C. §103(a) over Smith in View of Mitchell, Burgoyne, and the Whatman Filter Paper Overview is Traversed

The Examiner has rejected claim 22 under 35 U.S.C. 103(a) as allegedly unpatentable over Smith et al. (U.S. Patent 6,645,717; issued November 11, 2003; "Smith") as evidenced by Burgoyne (U.S. Patent 5,496,562; issued March 5, 1996; "Burgoyne") and Mitchell et al. (WO 00/21973; published April 20, 2000; "Mitchell"), as applied to claim 1 above and further in view of Qiagen Genomic DNA Handbook (pages 17-22, August 2001; "Qiagen"). Applicants traverse the rejection and respectfully request reconsideration of this claim.

The Patent Office alleges, in pertinent part:

> The teachings of Smith et al. are set forth in section 4 above. Smith et al. do not disclose the limitations of claim 22.

> Regarding claim 22 Qiagen protocol for genomic DNA purification from whole blood teaches sequential lysis of first blood cell membranes, washing away the debris from the nucleic and then lysing the cleaned nuclei to obtain genomic DNA (pages 21-22).
>
> Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used a two-step cell lysis protocol of Qiagen in the method of obtaining genomic DNA from the whole blood of Smith et al. The motivation to do so would have been that such protocol allowed purification of nuclei away from cell contaminants, which might interfere with subsequent reactions in which the DNA was used, such as PCR. [P. 9.]

Applicants respectfully traverse this rejection.

For the reasons discussed at length above with respect to the rejection of claim 1, Applicants also respectfully assert that claim 22 would not have been obvious to one of ordinary skill in the art over Smith, either alone or in combination with Mitchell and/or Burgoyne.

For reasons already discussed above and of record, Applicants respectfully submit that Mitchell ***teaches away from*** Smith.

Moreover, the teachings of Qiagen fail to supply the deficiencies of Smith, Mitchell and/or Burgoyne.

Applicants respectfully submit that claim 22 fulfills the requirements of 35 U.S.C. §103(a), thereby placing this claim in condition for allowance, and request the Examiner's reconsideration accordingly.

VI. Additional Remarks

If any issues are still remaining, in order to expedite prosecution and allowance of this application, Applicants request an interview with the Examiner. The Examiner is invited to contact the undersigned to schedule an interview at her earliest convenience.

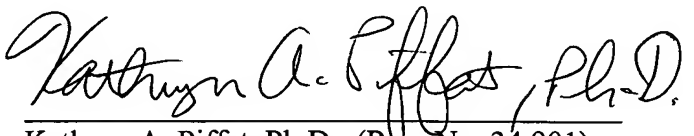
CONCLUSION

It is believed that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants hereby request a three-month extension of time for the Amendment and accompanying materials. If, however, a petition for an additional extension of time is required, then the Examiner is requested to treat this as a conditional petition for an additional extension of time and the Commissioner is hereby authorized to charge our deposit account no. 04-1105 for the appropriate fee. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,



Date: November 23, 2010

Kathryn A. Piffat, Ph.D., (Reg. No. 34,901)
EDWARDS ANGELL PALMER & DODGE, LLP
P.O. Box 55874
Boston, Massachusetts 02205
Telephone: 617-239-0100
Facsimile: 617-227-4420

Customer No.: 21874